REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing revisions and the following commentary.

This amendment adds and changes claims. A detailed listing is presented, with an appropriate status identifier, of all claims that are or were in the application, irrespective of whether any given claim remains under examination. After the claims are revised as set forth above, claims 1-12 and 37-40 will be pending.

1. THE INVENTOR DECLARATION UNDER RULE 1.67(A)

Applicants request that the Office withdraw its objection to the declaration. Inventor Louis D. Falo, Jr., entered changes in his address when he executed the declaration. The Office has identified no authority for the proposition that such changes must be initialed.

2. ENABLEMENT UNDER 35 U.S.C. § 112, ¶ 1

Claims 1-12 stand rejected "as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." Office action, page 2, lines 24-27. Applicants respectfully traverse this rejection.

A. THE OFFICE HAS NOT ESTABLISHED A *PRIMA FACIE* CASE OF NON-ENABLEMENT

A "specification...must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." *In re Marzocchi*, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971). Thus, the Office has the initial burden of challenging a presumptively correct assertion of utility in the disclosure. *Id.* 439 F.2d at 224, 169 U.S.P.Q. at 370. For the reasons identified below, the Office has failed to meet this burden.

The Office cited Bodey *et al.* to contend that "positive results achieved versus TAAs in animal models do not generally correlate with positive results in human." Office action, page 3,

last paragraph. In addition, the Office criticized applicants' *in vivo* data on the basis that "none of the experiments disclosed in the specification extend[s] beyond 2 or 3 months, thus is likely exacerbation of disease cannot be seen in the examples." *Id.* at page 4, second paragraph. Finally, the Office cited the Frank and the Cohen references as evidencing *a priori* unpredictability associated with the ability of the claimed formulations "to induce effective anti-virally-infected cell CTL-dependent immunity." *Id.* at page 5, fourth paragraph.

In essence, therefore, the Office has asserted non-enablement based on inoperability or lack of utility. For pharmaceutical inventions, however, Section 2107.03 of the M.P.E.P. warns of the difficulty associated with maintaining a rejection on the basis of inoperability.

> The Federal courts have consistently reversed rejections by the Office asserting a lack of utility for inventions claiming a pharmacological or therapeutic utility where an applicant has provided evidence that reasonably supports such a utility. In view of this, Office personnel should be particularly careful in their review of evidence provided in support of an asserted therapeutic or pharmacological utility.

The Office has conceded that "Examples 5 and 6 demonstrate efficacy of the invention in an animal model." Office Action, page 3, second paragraph. That should end the inquiry. The Federal Circuit has rejected, as a general proposition, the argument that *in vivo* tests in animals are not predictive of anti-cancer efficacy. *See In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1442 (Fed. Cir. 1995). In this regard, the Patent Statute requires only "statistically significant tests with standard experimental animals" to establish utility. *Id.*, *citing In re Krimmel*, 292 F.2d 948, 953, 130 U.S.P.Q. 215, 219 (C.C.P.A. 1961). The court also noted that the point at which a pharmaceutical invention becomes useful enough for a patent will often be long before it is ready for human use. To hold otherwise, noted the court, would raise the costs of obtaining patent protection for new inventions and remove the incentive to research fully and develop vital drugs and potential cures. *In re Brana*, 51 F.3d at 567-68, 34 U.S.P.Q.2d at 1442-43.

"Whether the specification would have been enabling as of the filing date involves consideration of the nature of the invention, the state of the prior art, and the level of skill in the art." M.P.E.P. § 2164.05(a). The evidence and explanation of record do not show that Bodey *et*

al., Frank *et al.* and Cohen reflect the existing state of the art when this application was filed. These references were published after the priority date of this application. The state of the art, however, does include numerous patents, granted by the Office before the filing date of this application, with claims drawn to vaccines against cancer and HIV. These patents demonstrate that the nature of the claimed formulations "does not suggest an inherently unbelievable undertaking or involve implausible scientific principles." *In re Brana*, 51 F.3d at 1566, 34 U.S.P.Q.2d at 1441. Even Bodey *et al.* recognizes some utility to cancer vaccines, concluding that "such four-modality immunotherapeutical approaches should not be limited to advanced, terminal cases, after all traditional modalities have been exhausted, but rather should be used in close conjunction with radiation and chemotherapeutical regimens to ensure the greatest possible benefit to the patient" (page 2674, first paragraph).

Current research dispels any doubt that the Bodey, Frank, and Cohen publications might cast on the utility of the claimed formulations. For example, the results of a recent phase I clinical trial have demonstrated that a dendritic-cell vaccine for renal cancer is safe and effective in boosting cancer patients' immune systems. See Duke University news release of May 1, 2003 (copy enclosed). Also, a dendritic cell vaccine for simian immunodeficiency virus (SIV) has been recently shown to elicit effective and durable SIV-specific cellular and humoral immunity. See Wu *et al.*, *Nat. Med.* 9: 27-32, 2003 (copy enclosed).

B. IN ANY EVENT, THE ALLEGED *PRIMA FACIE* CASE OF NON-ENABLEMENT IS OVERCOME BY EVIDENCE OF RECORD

According to the Federal Circuit, the test for enablement is whether the experimentation needed to make or use the invention is "undue." *See In re Wands*, 858 F.2d 731, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988). A "considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." 858 F.2d at 737, 8 U.S.P.Q.2d at 1404 (Fed. Cir. 1988). Not everything necessary to practice the invention need be disclosed. In fact, what is well-known is best omitted. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991).

To carry out the claimed invention, a person of skill in the art would need to know (1) how to prepare the claimed formulation comprising a macrophage or dendritic cell fused to a tumor cell or a virally infected cell and (2) how to administer the formulation to a patient. The application provides extensive directions on preparing the claimed formulations, as evidenced in Examples 1 and 2, *inter alia*. Assays for assessing anti-viral immunity were well known in the art at the time this application was filed. The application plainly explains how to administer the formulation (see paragraph bridging pages 9-10). The application therefore provides sufficient guidance for persons of ordinary skill in the art to practice the claimed invention without undue experimentation.

In light of the foregoing reasons, applicants respectfully request withdrawal of this rejection.

3. THE REJECTIONS UNDER 35 U.S.C. § 102

The Office has not rejected claims 4 and 9 over the art of record.

The Office has rejected claims 1-3 and 5-6 as anticipated by Peters *et al.*, *Immunobiology* 157: 261 (1980). Peters is a single-paragraph note, 16 lines in length, which speaks of isolating a cell type from peripheral human blood. Peters states that "a subset of previously attached cells has now detached .... These cells are reminiscent of dendritic cells from mouse spleen."

It is axiomatic that a proper § 102(b) reference must meet all the recited elements of the claim in question. Here, Peters discloses not dendritic cells but simply cells that are "reminiscent" thereof. That falls far short of the teaching needed to satisfy § 102. Applicants therefore request that the Office withdraw this ground of rejection.

The Office has rejected claims 1-3, 5-8 and 10-12 under 35 U.S.C. § 102(a) over WO 96/30030. Applicants have obviated this ground of rejection by submitting a declaration under 37 C.F.R. § 1.132, antedating the reference. This declaration was filed originally in related U.S. application serial No. 09/864,451, which claims the same priority as the present application. The declaration states that the invention embodied in the present claims was completed in this country before October 3, 1996, which is the publication date of WO 96/30030. Accordingly, the

latter document is not prior art as to the present claims. Applicants request that this ground of rejection be withdrawn.

Applicants believe that the present application is in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned, should he feel that some issue requires further consideration.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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By _____

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